IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

10X GENOMICS, INC. and PRESIDENT AND FELLOWS OF HARVARD COLLEGE, Plaintiffs, v. NANOSTRING TECHNOLOGIES, INC., Defendant.	)	C.A. No. 22-261 (MFK) DEMAND FOR JURY TRIAL

FIRST AMENDED COMPLAINT

Plaintiffs 10x Genomics, Inc. ("10x") and President and Fellows of Harvard College ("Harvard") allege in their First Amended Complaint for patent infringement against Defendant NanoString Technologies, Inc. ("NanoString") as follows:

NATURE OF THE ACTION

1. This is an action for infringement of U.S. Patent Nos. 10,227,639 ("the 639 Patent"), 11,021,737 ("the 737 Patent"), 11,293,051 ("the 051 Patent"), 11,293,052 ("the 052 Patent"), and 11,293,054 ("the 054 Patent") (collectively, the "Asserted Patents"). This action arises under the patent laws of the United States, Title 35, United States Code, including 35 U.S.C. § 271.

THE PARTIES

2. 10x is a Delaware corporation with its principal place of business at 6230 Stoneridge Mall Road, Pleasanton, CA 94588.

3. 10x is a pioneering innovator of genomics and sequencing technologies that are providing life science researchers and clinicians an unprecedented understanding of biology. By elegantly combining its proprietary hardware, chemistry, and software, 10x has developed and brought to market award-winning products that give single cell and spatial views of complex biological systems. 10x's products have enabled previously infeasible forms of research in the life

sciences in areas of critical importance to human health, including cancer research, neuroscience, immunology, infectious disease, and developmental biology.

4. Harvard is a Massachusetts educational institution with a principal place of business in Cambridge, MA. Harvard is a patent owner and licensor for the Asserted Patents.

5. On information and belief, NanoString is a Delaware corporation with its principal place of business in Seattle, WA.

6. NanoString makes, uses, sells, offers to sell, exports, and/or imports in the United States products, services, and components that have been and are used to infringe one or more claims of the Asserted Patents.

JURISDICTION AND VENUE

7. Plaintiffs incorporate the foregoing paragraphs of the Complaint by reference as if fully set for herein.

8. This civil action for patent infringement arises under the patent laws of the United States, 35 U.S.C § 1 *et seq.*, including in particular under 35 U.S.C. § 271. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

9. This Court has personal jurisdiction over Defendant, and venue is proper in this district pursuant to 28 U.S.C. § 1400(b), because NanoString is a Delaware corporation and thus resides in this district.

BACKGROUND

A. 10x's Groundbreaking Single Cell and Spatial Technologies

10. 10x is a life sciences technology company founded in 2012 in Pleasanton, California by Drs. Serge Saxonov and Benjamin Hindson. Since its inception, 10x has focused on building new technologies to enable breakthrough discoveries and accelerate the understanding of biology. To date, 10x has invested hundreds of thousands of hours and approximately $1 billion

in research and development to invent, design, and develop its proprietary line of products for understanding biology at unprecedented resolution and scale. 10x continues to invest significant time and money to further innovate and bring ground-breaking new products and capabilities to market.

11. 10x is now a worldwide leader in genomics, the comprehensive study of biological systems at a molecular and cellular level. Since 10x's first commercial launch in 2015, 10x's expanding suite of products has fueled a revolution in genomics, winning wide acclaim and commercial success. 10x has achieved an installed base of more than 3,500 instruments around the world, including at all of the top 100 global research institutions and all of the top 20 global biopharmaceutical companies. In 2021, annual sales of 10x products exceeded $490 million, a 64% increase over 2020.

12. Over 3500 scientific articles have been published based on data generated from 10x products, including hundreds of articles in top journals such as *Cell*, *Science*, and *Nature*. This scientific work details the use of 10x products to discover, for example: molecular mechanisms that lead to brain, breast and lung cancers; how the immune system reacts to COVID-19 infection; and a new type of lung cell that causes cystic fibrosis. The paradigm-changing nature of 10x's products has led to numerous accolades, including seven 10x products being named to *The Scientist* magazine's Top 10 Innovations list between 2015 and 2021.

13. 10x's Chromium platform has been essential to enabling single cell genomics—the study of biology at a cell-by-cell resolution and at a massive, system-wide scale, ushering in a single-cell revolution hailed by *Science* magazine as the 2018 "Breakthrough of the Year." Whereas traditional biology relies on "bulk analysis" in which tissue is analyzed as averages across the sample, 10x's breakthrough single cell products enable researchers to analyze samples on a

single cell basis—for millions of cells per experiment—thereby preserving information that is specific to each cell in the sample. 10x's single cell products do this by putting a different "tag" (a nucleic acid barcode) on each single cell in a sample, which can then be analyzed using sequencers to read the contents. The Chromium X, which launched in July 2021 and enables expansion of single cell studies to million-cell experiments, is the latest addition to 10x's award-winning platform and was named a Top 10 Innovation in 2021 by *The Scientist* magazine. https://www.the-scientist.com/features/2021-top-10-innovations-69438.

14. 10x, through its Spatial Transcriptomics and later Visium products, has catalyzed the field of spatial analysis by providing commercial offerings that enable true spatial discovery. Spatial analysis allows the large-scale interrogation of biological analytes with their spatial context. In contrast to traditional techniques in which analytes from a biological tissue are blended and analyzed as an average from various parts of the tissue, spatial analysis preserves information about the positions of the analytes in the tissue. This allows researchers and clinicians to build a comprehensive map—a kind of Google Earth—of where each analyte is, so that function can be tied to location. 10x's innovative spatial products use a tagging approach, analogous to that used in its single cell products, where the tags indicate the location of the analyte in the tissue rather than the cellular origin of the analyte. In 2020, *Nature Methods* named spatially resolved transcriptomics its "Method of the Year" and featured 10x's spatial technology on the cover. *See* https://www.nature.com/articles/s41592-020-01033-y. The 10x Visium Spatial Gene Expression product was named among the *Scientist* magazine's Top 10 Innovations in 2020. The power of Visium was again acknowledged in the February 2022 issue of *Science Translational Medicine*, in which a Visium study was a featured article and provided the cover illustration. *See* https://www.science.org/toc/stm/14/632.

B. 10x Invests In Developing *In Situ* Technologies

15. Most current molecular analyses, including single cell and spatial technologies, involve removing molecules from their native environment for analysis. *In situ* analysis, by contrast, aims to measure and analyze a large number of molecules directly in tissue samples and capture the precise location of those molecules at sub-cellular resolution.

16. In 2020, 10x announced its acquisition of ReadCoor, Inc., founded based on George Church's work at Harvard, obtaining intellectual property, key technology advances, and deep talent and expertise in the emerging *in situ* field.

17. 10x Genomics is currently developing Xenium In Situ, 10x's forthcoming platform built from its investments in *in situ* technology. Xenium In Situ will be a complete platform—including the Xenium In Situ Analyzer instrument, Xenium In Situ reagents and panels, Xenium software, and the full support of 10x's team of spatial experts—designed to create spatial maps of gene expression in the original tissue at true cellular and subcellular resolutions.

C. NanoString's Infringing CosMx SMI Platform and Technology Access Program

18. Nearly half a year after 10x's widely observed acquisition, NanoString announced the launch of its Technology Access Program for the Spatial Molecular Imager in March 2021. On November 9, 2021, NanoString announced its new, commercially-branded CosMx Spatial Molecular Imager (SMI), which is purported to provide spatially resolved mapping data and imaging for RNA and protein at a single-cell and subcellular resolution. NanoString markets the CosMx SMI as providing "high-plex *in situ* spatial analysis" with "quantification and visualization of up to 1,000 RNA and 100 validated protein analytes." https://www.nanostring.com/products/cosmx-spatial-molecular-imager/overview/. Through its

CosMx SMI Technology Access Program ("CosMx TAP"), NanoString offers to its customers an *in situ* spatial molecular imaging service using its CosMx SMI platform.

19. NanoString practices the Asserted Patents by using the CosMx SMI workflow on behalf of its own scientists and researchers and for its CosMx SMI TAP customers. Through the CosMx SMI TAP, customers submit tissue samples to NanoString's Translational Services Lab. NanoString processes samples using its CosMx SMI platform and provides customers with reports including raw data and analyzed results. *See* https://www.nanostring.com/products/cosmx-spatial-molecular-imager/technology-access-program/. On information and belief, NanoString also advertises and offers the CosMx SMI platform for sale for early access customers interested in ordering the platform for delivery in 2022. *See* https://www.nanostring.com/products/cosmx-spatial-molecular-imager/technology-access-program/.

20. The "Accused Instrumentalities" are all products, components, and services that are made, used, performed, offered to sell, sold, and/or imported into the United States by or on behalf of NanoString in connection with NanoString's CosMx Spatial Molecular Imaging ("CosMx SMI") platform. The Accused Instrumentalities include, for example and without limitation, products, components, and services used or provided by NanoString in connection with its CosMx SMI Technology Access Program.

D. The Patents In Suit

21. Through the development and subsequent making, using, selling, offering for sale, and/or importing of the Accused Instrumentalities, NanoString has and continues to infringe the "Asserted Patents":

(a) U.S. Patent No. 10,227,639, entitled "Compositions and Methods for Analyte Detection" (Exhibit 1);

(b) U.S. Patent No. 11,021,737, entitled "Compositions and Methods for Analyte Detection" (Exhibit 2);

(c) U.S. Patent No. 11,293,051, entitled "Compositions and Methods for Analyte Detection" (Exhibit 3);

(d) U.S. Patent No. 11,293,052, entitled "Compositions and Methods for Analyte Detection" (Exhibit 4); and

(e) U.S. Patent No. 11,293,054, entitled "Compositions and Methods for Analyte Detection" (Exhibit 5).

22. The 639 Patent was duly and legally issued on March 12, 2019, by the United States Patent and Trademark Office. U.S. Application No. 14/366,486, which issued as the 639 Patent, claims the benefit of Application No. PCT/US2012/071398, filed on December 21, 2012, and Provisional Application No. 61/579,265, filed on December 22, 2011. Daniel Levner, Je-hyuk Lee, George M. Church, and Michael Super are named inventors on the face of the 639 Patent.

23. Harvard is the sole legal owner of the 639 Patent. A true and correct copy of the assignment abstract and record of the 639 Patent is attached as Exhibit 6. The 639 Patent is exclusively licensed to 10x, including *inter alia* the right to sue NanoString for its acts of infringement and to recover damages therefrom.

24. The 737 Patent was duly and legally issued on June 1, 2021, by the United States Patent and Trademark Office. U.S. Application No. 16/941,585, which issued as the 737 Patent, claims the benefit of Application No. PCT/US2012/071398, filed on December 21, 2012, Provisional Application No. 61/777,383, filed on March 12, 2013, and Provisional Application No. 61/579,265, filed on December 22, 2011. George M. Church, Je-hyuk Lee, Daniel Levner, and Michael Super are named inventors on the face of the 737 Patent.

25. Harvard is the sole legal owner of the 737 Patent. A true and correct copy of the assignment abstract and record of the 737 Patent is attached as Exhibit 7. The 737 Patent is

exclusively licensed to 10x, including *inter alia* the right to sue NanoString for its acts of infringement and to recover damages therefrom.

26. The 051 Patent was duly and legally issued on April 5, 2022, by the United States Patent and Trademark Office. U.S. Application No. 17/238,642, which issued as the 051 Patent, claims the benefit of Application No. PCT/US2012/071398, filed on December 21, 2012, Provisional Application No. 61/777,383, filed on March 12, 2013, and Provisional Application No. 61/579,265, filed on December 22, 2011. George M. Church, Je-Hyuk Lee, Daniel Levner, and Michael Super are the named inventors of the 051 Patent.

27. Harvard is the sole legal owner of the 051 Patent. A true and correct copy of the assignment abstract and record of the 051 Patent is attached as Exhibit 8. The 051 Patent is exclusively licensed to 10x, including *inter alia* the right to sue NanoString for its acts of infringement and to recover damages therefrom.

28. The 052 Patent was duly and legally issued on April 5, 2022, by the United States Patent and Trademark Office. U.S. Application No. 17/238,682, which issued as the 052 Patent, claims the benefit of PCT Application No. PCT/US12/71398, filed December 21, 2012, U.S. Provisional Application No. 61/579,265, filed December 22, 2011, and Provisional Application No. 61/777,373, filed March 12, 2013. George M. Church, Je-Hyuk Lee, Daniel Levner, and Michael Super are the named inventors of the 052 Patent.

29. Harvard is the sole legal owner of the 052 Patent. A true and correct copy of the assignment abstract and record of the 052 Patent is attached as Exhibit 8. The 052 Patent is exclusively licensed to 10x, including *inter alia* the right to sue NanoString for its acts of infringement and to recover damages therefrom.

30. The 054 Patent was duly and legally issued on April 5, 2022, by the United States Patent and Trademark Office. U.S. Application No. 16/393,215, which issued as the 054 Patent, claims the benefit of PCT Application No. PCT/US12/71398, filed December 21, 2012, and U.S. Provisional Application No. 61/579,265, filed December 22, 2011. Daniel Levner, Je-Hyuk Lee, George M. Church, and Michael Super are the named inventors of the 054 Patent.

31. Harvard is the sole legal owner of the 054 Patent. A true and correct copy of the assignment abstract and record of the 054 Patent is attached as Exhibit 9. The 054 Patent is exclusively licensed to 10x, including *inter alia* the right to sue NanoString for its acts of infringement and to recover damages therefrom.

COUNT I: Infringement of U.S. Patent No. 10,227,639

32. Plaintiffs incorporate and reallege paragraphs 1 - 31 above as if fully set forth herein.

33. NanoString has infringed and continues to infringe one or more claims of the 639 Patent, including without limitation claims 1-8, 10-13, 15-29, and/or 33-36, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority the Accused Instrumentalities and/or components thereof. Attachment A provides an exemplary infringement claim chart for one asserted claim and exemplary and/or representative Accused Instrumentalities.

34. Plaintiffs have suffered and continue to suffer damages as a result of NanoString's infringement of the 639 Patent.

35. Unless NanoString is enjoined from infringing the 639 Patent, NanoString's efforts to design, develop, market, offer to sell, and sell the Accused Instrumentalities will cause Plaintiffs to suffer irreparable injury for which damages are an inadequate remedy.

COUNT II: Infringement of U.S. Patent No. 11,021,737

36. Plaintiffs incorporate and reallege paragraphs 1 - 35 above as if fully set forth herein.

37. NanoString has infringed and continues to infringe one or more claims of the 737 Patent, including without limitation claims 1-6, 8-29, and/or 31-49, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority the Accused Instrumentalities and/or components thereof. Attachment B provides an exemplary infringement claim chart for one asserted claim and exemplary and/or representative Accused Instrumentalities.

38. Plaintiffs have suffered and continue to suffer damages as a result of NanoString's infringement of the 737 Patent.

39. Unless NanoString is enjoined from infringing the 737 Patent, NanoString's efforts to design, develop, market, offer to sell, and sell the Accused Instrumentalities will cause Plaintiffs to suffer irreparable injury for which damages are an inadequate remedy.

COUNT III: Infringement of U.S. Patent No. 11,293,051

40. Plaintiffs incorporate and reallege paragraphs 1 - 39 above as if fully set forth herein.

41. NanoString has infringed and continues to infringe one or more claims of the 051 Patent, including without limitation claim 1, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority the Accused Instrumentalities and/or components thereof. Attachment C provides an exemplary infringement claim chart for one asserted claim and exemplary and/or representative Accused Instrumentalities.

42. Plaintiffs have suffered and continue to suffer damages as a result of NanoString's infringement of the 051 Patent.

43. Unless NanoString is enjoined from infringing the 051 Patent, NanoString's efforts to design, develop, market, offer to sell, and sell the Accused Instrumentalities will cause Plaintiffs to suffer irreparable injury for which damages are an inadequate remedy.

COUNT IV: Infringement of U.S. Patent No. 11,293,052

44. Plaintiffs incorporate and reallege paragraphs 1 - 43 above as if fully set forth herein.

45. NanoString has infringed and continues to infringe one or more claims of the 052 Patent, including without limitation claim 1, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority the Accused Instrumentalities and/or components thereof. Attachment D provides an exemplary infringement claim chart for one asserted claim and exemplary and/or representative Accused Instrumentalities.

46. Plaintiffs have suffered and continue to suffer damages as a result of NanoString's infringement of the 052 Patent.

47. Unless NanoString is enjoined from infringing the 052 Patent, NanoString's efforts to design, develop, market, offer to sell, and sell the Accused Instrumentalities will cause Plaintiffs to suffer irreparable injury for which damages are an inadequate remedy.

COUNT V: Infringement of U.S. Patent No. 11,293,054

48. Plaintiffs incorporate and reallege paragraphs 1 - 47 above as if fully set forth herein.

49. NanoString has infringed and continues to infringe one or more claims of the 054 Patent, including without limitation claim 1, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making and/or using, offering to sell, selling, and/or importing into the United States without authority the Accused Instrumentalities and/or components thereof. Attachment E provides an exemplary infringement claim chart for one asserted claim and exemplary and/or representative Accused Instrumentalities.

50. Plaintiffs have suffered and continue to suffer damages as a result of NanoString's infringement of the 054 Patent.

51. Unless NanoString is enjoined from infringing the 054 Patent, NanoString's efforts to design, develop, market, offer to sell, and sell the Accused Instrumentalities will cause Plaintiffs to suffer irreparable injury for which damages are an inadequate remedy.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter the following relief in its favor and against NanoString:

A. For entry of judgment that the 639 Patent, 737 Patent, 051 Patent, 052 Patent, and 054 Patent have been and continue to be infringed by NanoString, either literally or under the doctrine of equivalents;

B. For a declaration that each of the Asserted Patents is valid and enforceable;

C. For permanent injunctions enjoining the aforesaid acts of infringement by NanoString, its officers, agents, servants, employees, attorneys, parent and subsidiary entities, assigns and successors in interest, and those persons acting in concert with them, including related individuals and entities, customers, representatives, distributors, and dealers. In the alternative, if the Court finds that an injunction is not warranted, Plaintiffs request an award of post-judgment royalty to compensate for future infringement;

D. An award of all monetary relief adequate to compensate for damages resulting from NanoString's infringement, including lost profits but in no event less than a reasonable royalty under 35 U.S.C. § 284 for NanoString's infringement, including all pre-judgment and post-judgment interest at the maximum rate allowed by law;

E. A declaration that the case is an exceptional case and that NanoString be required to pay Plaintiffs' attorneys' fees pursuant to 35 U.S.C. § 285; and

F. A judgment awarding Plaintiffs such other and further relief as the Court may deem just, reasonable, and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Plaintiffs hereby demand a jury trial on all issues so triable.

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